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(54) ESTERS OF PROSTAN-I-OL DERIVATIVES, PROCE 3S FOR THEIR MANUFACTURE AND PREPARATIONS CONTAINING THEM

(71) We, SCHERING AKTIEN-GESELLSCHAFT, a Body Corporate organised according to the laws of The Federal Republic of Germany, of Berlin and Bergkamen, The Federal Republic of Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

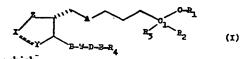
The present invention is concerned with new esters of prostan - 1 - ol derivatives and with their manufacture and use.

It is known that the physiological actions of prostaglandins both in the mammalian organism and in vitro are only of short duration, as they are rapidly converted into numerous pharmacologically inactive products of metabolism. It is also known that the natural prostaglandins possess no biological specificity, which is necessary for a medicament.

It has therefore been desired to develop prostaglandin analogues having an action spectrum comparable with that of natural prostaglandins and to bring about structural alterations by means of which the duration and selectivity of the activity is increased.

It has now been found that the prostan

1 - ol esters of the present invention as defined below, surprisingly possess an outstanding specificity of action and a longer duration of action than do natural prostaglandins. Thus, the compounds of the present invention exhibit, for example, a very good action on the uterus, while the intestinal and vascular musculature is practically unaffected. The present invention provides compounds of the general formula I



in which

R₁ represents an acyl group of an organic carboxylic or sulphonic acid containing

1 to 15 carbon atoms, a group obtainable from an oxygen-containing inorganic acid by the removal of a hydroxyl group, or a group of the formula



in which U represents an oxygen or sulphur atom and R₄ represents an optionally substituted alkyl, cycloalkyl, aryl or heteroaryl group or an acyl group of an organic carboxylic or sulphonic acid.

R₂ and R₃ each represents a hydrogen atom or an alkyl group containing 1 to 4 carbon atoms,

A represents a —CH₂—CH₂—, cis —CH=CH— or trans —CH=CH group,

B represents a —CH₂—CH₂—, trans —CH=CH— or —C≡C— group or a



group, in which the methylene group is α - or β -positioned,

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W represents a free, esterified or etherified hydroxy-methylene group, the hydroxyl group being in the α - or β -position, a free or ketalised carbonyl group or a group of the formula

CH=CH— OF --CH₂---CH---, R's

in which R, represents a free, esterified or etherified hydroxyl group in the a- or β-position,

in which R's represents an alkyl group or a free or etherified hydroxyl group. As a

D and E together represent a direct bond,

NH-R.

D represents a straight chained or branched alkylene group containing 1 to 5 carbon atoms or a —C≡C— group and

group there is to be understood a substituted carbamoyl or thiocarbamoyl group. As indicated above, the carbamoyl group or thiocarbamoyl group is substituted at the nitrogen atom by an optionally substituted alkyl, cycloalkyl, aryl or heteroaryl group or an acyl group of an organic carboxylic or sulphonic acid.

E represents an oxygen or sulphur atom or a direct bond,

> As alkyl groups represented by R. there come into consideration straight or branched alkyl groups containing 1 to 10 carbon atoms for example methyl, ethyl, propyl, isobutyl, butyl, pentyl, heptyl, hexyl and decyl groups.

R. represents an unsaturated aliphatic hydrocarbon group, an optionally C1--alkyl - substituted cycloalkyl group, an optionally substituted aryl - aliphatic hydrocarbon group, an optionally substituted aryl group, a benzodioxol - 2 yl group or a monocyclic heterocyclic group and, when D and E together repre-

The alkyl groups represented by Re may be substituted one or more times by halogen atoms, alkoxy groups, optionally substituted aryl groups, dialkylamino groups and trialkylammonium groups.

sent a direct bond, or D represents a straight channel or branched alkylene group containing 1 to 5 carbon atoms or a —C≡C— group and E represents an oxygen or sulphur atom or D represents 30 a —C≡C— group and E represents a direct bond, may also represent an alkyl

As substituents there may be mentioned, for example, fluorine, chlorine, bromine, phenyl, dimethylamino, diethylamino, methoxy and ethoxy.

Z represents a carbonyl or a free, esterified or etherified hydroxymethylene group, and

As preferred optionally substituted alkyl groups represented by R₆ there should be mentioned methyl, ethyl, propyl, isobutyl, butyl, trichloromethyl and trifluoromethyl groups.

Cycloalkyl groups represented by R, are preferably such groups containing 3 to 8 carbon atoms, for example cyclobutyl, cyclopentyl and cyclohexyl groups, but preferably

when Z represents a free esterified or etherified hydroxymethylene represents a

a cyclopropyl group.

As aryl and heteroaryl groups represented by R_s there come into consideration both substituted and unsubstituted aryl groups and heteroaryl groups, for example phenyl, 1 - naphthyl and 2 - naphthyl groups, each of which may be substituted by 1 to 3 halogen atoms, a phenyl group, 1 to 3 alkyl groups each containing 1 to 4 carbon atoms, of a chloromethyl, fluoromethyl, trifluoromethyl or alkoxy group, and thienyl, furyl and pyridyl alkoxy group, and thienyl, furyl and pyridyl groups. Substitution is preferably in the 3-and/or 4-position(s) of the phenyl ring, for example, by fluorine, chlorine, alkoxy or tri-

group, in which the methylene group is α - or β -positioned, or a group of the formula

> fluoromethyl. As acyl groups represented by R₁ and R₆ there come into consideration physiologically tolerable acyl groups, Preferred acids from which the acyl groups are derived are organic carboxylic acids and sulphonic acids containing 1 to 15 carbon atoms, which belong to the

in which R₃ represents an alkyl group or a free, esterified or etherified hydroxyl group, or, when Z represents a carbonyl group, represents a group of the formula

aliphatic, cycloaliphatic, aromatic, aromatic aliphatic or heterocyclic series. These acids may be saturated or unsaturated and/or polybasic and/or substituted in the usual manner. As examples of substituents there may be mentioned alkyl, hydroxyl, alkoxy, oxo or

amino groups or halogen atoms.

By way of example there may be mentioned the following carboxylic acids: Formic acid, acetic acid, propionic acid, butyric acid, isobutyric acid, valeric acid, isovaleric acid, caproic acid, oenanthic acid, caprylic acid, perlargonic acid, capric acid, undecanoic acid, lauric acid, tridecanoic acid, myristic acid, pentadecanoic acid, trimethylacetic acid, diethylacetic acid, tert.-butylacetic acid, cyclopentylacetic acid, cyclohexylacetic acid, cyclohexane, carboxylic acid, phenylacetic acid, phenoxyacetic acid, methoxyacetic acid, ethoxyacetic acid, mono- and di- and trichloracetic acids, aminoacetic acid, diethylaminoacetic acid, piperidinoacetic acid, morpholinoacetic acid, lactic acid, succinic acid, adipic acid, benzoic acid, benzoic acids substituted by halogen, trifluoromethyl, hydroxyl, alkoxy or carboxyl groups, nicotinic acid, isonicotinic acid, furan - 2 - carboxylic acid and cyclopentyl - propionic acid. Especially preferred acyl groups are those containing up to 10 carbon atoms.

As sulphonic acids there come into consideration, for example, methane sulphonic acid, ethane sulphonic acid, isopropyl sulphonic acid, β -chlorethane sulphonic acid, butane sulphonic acid, cyclopentane sulphonic acid, cyclohexane sulphonic acid, benzene sulphonic acid, para - toluene sulphonic acid, para - chlorobenzene sulphonic acid, N,N dimethylamino - sulphonic acid, N,N - diethylamino - sulphonic acid, N,N - bis - (B chlorethyl) - aminosulphonic acid, N,N - diisobutylamino - sulphonic acid, N,N - di-butylamino - sulphonic acid and pyrrolidino-, piperidino- piperazino-, N - methylpiperazinoand morpholino - sulphonic acids.

There also come into consideration for R₁

acyl groups derived from the usual inorganic acids, for example sulphuric and phosphoric

acids.

As alkyl groups represented by R2 and R3 there come into consideration straight and branched-chained alkyl groups containing 1 to 4 carbon atoms, for example methyl, ethyl, propyl, isopropyl, butyl, isobutyl and tert. butyl groups. Preferred are methyl and ethyl

groups.

The hydroxyl group represented by R_s and those in groups represented by W and Z may be functionally converted by etherification or esterification, and the hydroxyl group represented by R'₅ may be functionally converted by etherification; the free or functionally converted hydroxyl groups in groups represented by W and Z may be α - or β -

As ether-forming and acyl groups for such functional conversion there come into consideration the groups known to the expert. Preferred are ether-forming groups capable of being easily split off, for example tetrahydropyranyl, tetrahydrofuranyl, α - ethoxyethyl, trimethylsolyl, dimethyl - tert. - butyl silyl and tri - parabenzyl - silyl groups. As acyl groups there come into consideration the same as those given above for R₁, and there may be mentioned especially, for example, acetyl, propionyl, butyryl and benzoyl groups.

When W represents a carbonyl group, the latter may be functionally converted by ketalisation. Especially suitable is the preparation of cyclic ketals containing 1 to 3 carbon atoms in the ring, for example with ethylene glycol, 1,3 - propanediol, 2,2 - dimethyl - 1,3 - propanediol, cyclopentane - 1,2 diol

or glycerine.

As aliphatic hydrocarbon groups and optionally substituted aryl - aliphatic hydrocarbon groups represented by R, there come into consideration straight and branched-chained, saturated and unsaturated aliphatic hydrocarbon groups, preferably saturated, containing 1 to 10 and especially 1 to 6 carbon atoms, which are optionally substituted by optionally substituted aryl. There may be mentioned, for example, methyl, ethyl, propyl, butyl, isobutyl, tert. - butyl, pentyl, hexyl, heptyl, octyl, butenyl, isobutenyl, propenyl,

pentenyl, benzyl and parachlorobenzyl groups. The cycloalkyl group represented by R. may contain in the ring 4 to 10, and preferably 5 to 6, carbon atoms. The rings may be substituted by alkyl groups containing 1 to 4 carbon atoms. There may be mentioned, for example, cyclopentyl, cyclohexyl, methyl -

cyclohexyl and adamantyl groups.

As substituted or unsubstituted aryl groups represented by R, there come into consideration, for example, phenyl, 1 - naphthyl and 2 - naphthyl groups, each of which may be substituted by 1 to 3 halogen atoms, a phenyl group, 1 to 3 alkyl groups each containing 1 to 4 carbon atoms, or a chloromethyl, fluoro methyl, trifluoromethyl, carbonyl, alkoxy or hydroxyl group.

Preferably the substitution is in the 3and/or 4-position(s) of the phenyl ring, for example by fluorine, chlorine, alkoxy or trifluoromethyl, or in the 4-position by hydroxyl.

As alkyl groups represented by Rs and R's there come into consideration alkyl groups containing 1 to 2 carbon atoms, preferably

methyl groups.

As monocyclic heterocyclic groups represented by R, there come into consideration 5and 6-membered heterocycles, which contain at least one hetero-atom, preferably nitrogen, oxygen or sulphur. By way of example there may be mentioned 2-furyl, 2-thienyl, 2-pyridyl, 3-pyridyl or 4-pyridyl.

The present invention also provides a pro-

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cess for the manufacture of the new esters of prostan - 1 - ol derivatives of the general formula I, wherein a compound of the general formula II

in which A, Z,

X----X

B, W, D, E, R₂, R₃ and R₄ have the meanings given above, is esterified in the 1-position if desired after protecting any other free hydroxyl group present, and then, if desired, in the resulting compound any protected hydroxyl group is liberated and/or any free hydroxyl group is oxidized or esterified and/or any free keto group is ketalised or reduced and/or any double bond is hydrogenated or methylenated and/or by splitting off water in the 10,11 - position from an 11 - hydroxy - 9 - oxo - compound a double bond is introduced, and/or, if desired, any epimers are separated.

The esterification of the alcohols of the general formula II may be carried out in a manner known per se. For example, the esterification is carried out by reacting an acid derivative, preferably an acid halide or acid anhydride, in the presence of a base, for example sodium hydride, pyridine, triethylamine, tributylamine or 4 - dimethylaminopyridine, with an alcohol of the general formula II. The reaction may be carried out without a solvent or in an inert solvent, preferably acetone, acetonitrile, dimethylacetamide or DMSO, at temperatures above or below room temperature, for example between -80°C and 100°C, and preferably at room temperature.

Furthermore, for example, an alcohol of the general formula II may be reacted with an isocyanate or thioisocyanate of the general formula III

$$U=C=N-R_c \qquad (III)$$

in which

U and R_a have the meanings given above, optionally with the addition of a tertiary amine, for example triethylamine or pyridine. The reaction may be carried out without a solvent or in an inert solvent, preferably acetone, acetonitrile, dimethylacetamide, methylene chloride, tetrahydrofuran, diethyl ether, benzene, toluene or DMSO, at temperatures above or below room temperature, for example between —80°C and 100°C, and preferably at 0 to 30°C.

When the starting material contains, in

When the starting material contains, in addition to the hydroxyl group in the 1-position, additional hydroxyl groups in the pro-

stane group, these hydroxyl groups are also esterified in accordance with the process of the present invention. When final end products are desired, in which additional hydroxyl groups in the prostane group are present in the form of free hydroxyl groups, it is of advantage to start from starting materials in which these are intermediately protected preferably by ether-forming groups capable of being split off easily. When there are used as starting materials compounds which contain in the prostane group esterified or etherified hydroxyl groups, these groups in the end product may be esterified, after liberating the esterified or etherified hydroxyl groups, and different acyl groups may be introduced into the end product.

The liberation of esterified or etherified hydroxyl groups is carried out by known methods. For example, the splitting off of hydroxyl-protecting groups, for example, the tetrahydropyranyl group, is carried out in an aqueous solution of an organic acid, for example acetic acid or propionic acid, or in an aqueous solution of an inorganic acid, for example hydrochloric acid or tetrabutylammonium fluoride. In order to improve solubility it is of advantage to add an inert organic solvent miscible with water. Suitable organic solvents are, for example, alcohols, for example methanol and ethanol, and ethers, for example dimethoxyethane, dioxane and tetrahydrofuran. Tetrahydrofuran is preferably used. The splitting is preferably carried out at tempeatures between 20°C and 80°C

The ketalisation is carried out in a manner known per se, for example, by heating with ethylene glycol in the presence of an acid catalyst with the separation of water. As acid catalysts there are especially suitable paratoluene sulphonic acid and perchloric acid.

The oxidation of hydroxyl groups present is carried out by methods known per se with the usual oxidizing agents. For example, oxidation of the 9 - hydroxyl group to form the ketone may be carried out with Jones reagent (J. Chem. Soc. 1953, 2555). An excess of the oxidizing agent is used in a suitable diluent, for example acetone, at temperatures between 0°C and -50°C, and preferably at -20°C. The reaction generally terminates after 5 to 30 minutes. The oxidation is preferably carried out after intermediate protection of 11- and 15-hydroxyl groups, for example, by silylation (Chem. Comm. (1972), 1120). The silylation is carried out, for example, with N,N - diethyl - trimethylsilyl amine in acetone at -70°C to +20°C, and preferably at -40°C to 0°C. As further oxidizing agents there are suitable silver carbonate on "Celite" (Registered Trade Mark) or Collins reagent (Tetrahedron Leters, 1968, 3363).

The selective oxidation of 9,11-di-hydroxy-compounds, which contain no oxidizable

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hydroxyl group in the 15-position, is carried out by methods known to the expert.

For the oxidation of the 11α -hydroxyl group there is preferably used Jones reagent or Collins reagent, and the selective oxidation of the 9\a-hydroxyl group is carried out with Fetizon reagent (Tetrahedron 29, 2867 (1973)), silver carbonate or platinum/oxygen (Adv. in Carbohydrate Chem. 17, 169 (1962)). The oxidation with Jones reagent is carried out at -40°C to +20°C, and preferably at -30° C to -10° C, or with Collins reagent at -20° C to 30° C, and preferably at 0° C to 20° C, in a solvent inert to the oxidizing agent. As solvents there may be used methylene chloride, chloroform, ethylene chloride and pyridine, but preferably methylene chloride.

As solvents for the oxidation with Fetizon reagent, silver carbonate or platinum with oxygen there may be used benzene, toluene, xylene, ethyl acetate, acetone, tetrahydro-furan, diethyl ether and dioxane and other inert solvents. The reaction temperatures are between 20°C and 110°C in the case of the silver carbonate or Fetizon oxidation, and preferably at the boiling temperature of the solvent. In the oxidation with platinum/oxygen temperatures of preferably 20°C to 50°C are used.

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The reduction of the 9-keto group is carried out with the usual reducing agents; for example, it is reduced with sodium borohydride, lithium tri - tert. - butoxy - aluminium hydride, zinc borohydride or aluminium isopropylate in the presence of an alcohol, or potassium tri - sec. - butyl borohydride, and preferably with sodium borohydride at temperatures between -50°C and +50°C, and preferably at 0°C to 20°C. As solvent for this reaction there come into consideration depending on the reducing agent used, methanol, ethanol, isopropanol, diethyl ether, dioxane and tetrahydrofuran. In the reduction with sodium borohydride there is preferably used methanol, ethanol or isopropanol. The α - and β - hydroxyl - epimeric mixture formed may be separated in the usual manner by column or layer chromatography.

If it is desired to reduce O=C double bonds present in the primary product, the hydrogenation is carried out by methods

known per se.

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The hydrogenation of the 5,6-double bond is carried out in a known manner at low temperatures, preferably at -20° C, in an atmosphere of hydrogen in the presence of a noble metal catalyst. There is suitable as catalyst, for example, 10% palladium on charcoal.

If both 5,6- and 13,14 - double bonds are to be hydrogenated, the operation is carried out at a higher temperature, preferably at

The dehydration of a 9 - oxo - compound,

in which the 11 - hydroxyl group and a hydrogen atom in the 10-position are split off to form a prostaglandin-A derivative, may be carried out under conditions that are generally known to the expert. In general the dehydration is carried out in a solution of an organic acid, for example acetic acid, or an inorganic acid, for example hydrochloric acid, at temperatures between 20°C and 80°C. The reaction terminates after 2 to 17 hours.

The methylenation of the 10,11- and/or 13,14-double bond(s) is carried out in the case of the 9-oxo- or 15-oxo-compounds by methods known per se. For example, there may be mentioned reaction with diazo hydrocarbons, optionally in the presence of metal salts, reaction with dimethyl-sulphoxonium methylide and reaction according to the Simmons-Smith method with zinc

methylene dihalides.

A preferred method consists in reacting the above mentioned compounds with diazo-hydrocarbons, for example diazomethane, diazoethane and diazopropane, but preferably diazomethane. The reaction is carried out, for example, in the presence of metal salts at temperatures between 20°C and -100°C, and preferably at 0°C, in an inert solvent, for example diethyl ether, tetrahydrofuran, glyme, diglyme or dioxane, but preferably in diethyl ether. As metal salts there may be used copper chloride, copper acetate, palladium-(II) acetate, and palladium-(II) chloride, but preferably palladium-(II) acetate.

The separation of the epimers is carried out by methods known to the expert, for example by a column or layer chromatography or by fractional crystallization.

The preparation of compounds of the general formula II in which R₂ and R₃ each represents a hydrogen atom is carried out by the usual methods, for example, by reducing a corresponding prostanoic acid derivative to form a primary alcohol. Preferable is the reaction of prostanoic acid esters with lithium aluminium hydride.

The preparation of the new compounds of the general formula II, in which R2 represents an alkyl group containing 1 to 4 carbon atoms and R_s represents a hydrogen atom, is carried out in the usual manner, for example, by reduction of a prostanoic acid derivative to form the aldehyde. The reduction is preferably carried out upon prostanoic acid esters with diisobutyl-aluminium hydride at -70°C to -40°C in an inert solvent, for example toluene. The subsequent reaction of the aldehyde with a lithium alkyl yields at 0°C in an inert solvent, preferably in diethyl ether and tetrahydrofuran mixtures, the secondary alcohols of the general formula II.

The preparation of the new compounds of the general formula II, in which R₂ and R₃ each represents an alkyl group containing 1 to 4 carbon atoms, is carried out by the usual 130

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	methods, for example, by reaction of a pro-	oxy
	stanoic acid ester with a lithium alkyl at	me (
	temperatures between -10°C and +10°C, and preferably at 0°C, in an inert solvent, for	pio
5	example diethyl ether and tetrahydrofuran	pro
	mixtures, with the formation of tertiary	(
	alcohols of the general formula.	pro
	When free hydroxyl groups are desired in	pro
	the end product, it is of advantage, before the	Ca
10	reduction to the C ₁ -alcohols, to intermediately	17,
	protect the optionally present free hydroxyl or free oxo groups, for example, by etherifica-	9,1
	tion or ketalisation, respectively.	(
•	Preferred compounds of the present inven-	Car
15	tion are, not only the compounds mentioned	16
	in the Examples below, but also the follow-	pro
	ing compounds:	Ca
	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (2 -	me
20	Carboxy - propionyloxy) - prosta - 5,13 - dien - 9,11,15 - triol.	pro
20	(5Z,13E) - (8R,11R,12R,15S) - 1 - (2 -	Ca:
	Carboxy - propionyloxy) - 11.15 - dihydroxy -	16
	prosta - 5,13 - dien - 9 - one.	17,
26	(5Z,13E) - (8R,9S,11R,12R,15S,16RS) - 1 -	9 -
25	(2 - Carboxy - propionyloxy) - 16 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.	Cai
	5Z,13E) - (8R,11R,12R,15S,16RS) - 1 -	pho
	(2 - Carboxy - propionyloxy) - 11,15 - di-	5,1
20	hydroxy - 16 - methyl - prosta - 5,13 - dien -	(
30	9 - one. (57.13F) - (8P.120.150) 1 Mathematical	Car
	(5Z,13E) - (8R,12S,15S) - 1 - Methoxy- acetoxy - 15 - hydroxy - prosta - 5,10,13 -	16 teti
	trien - 9 - one.	(
	(5Z,13E) - (8R,12S,15S) - 1 - (2 - Carb-	Ca
35	oxy - propionyloxy) - 15 - hydroxy - prosta -	ph
	5,10,13 - trien - 9 - one. (5Z,13E) - (8R,12S,15S,16RS) - 1 - (2 -	5,1
	Carboxy - propionyloxy) - 16 - methyl - 15 -	Ca
	hydroxy - prosta - 5,10,13 - trien - 9 - one.	16
40	(32,13E) - (8K,125,13K) - 1 - (2-Carboxy-	tet
	propionyloxy) - 16,16 - ethylene - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.	C-
	(13E) - (8R,12S,15S) - 1 - Methoxyacet-	Ca ph
	oxy - 15 - hydroxy - prosta - 10,13, - dien -	5,1
45	9 - one.	(
	(13E) - (8R,12S,15S) - 1 - (2 - Carboxy -	Ca
	propionyloxy) - 15 - hydroxy - prosta - 1,13 - dien - 9 - one.	16 tet
	(13E) - (8R,12S,15R) - 1 - (2 - Carboxy -	tri
50	propionyloxy) - 15 - hydroxy - 16,16 - di-	
	methyl - prosta - 10,13 - dien - 9 - one.	Ac
	(13E) - (8R,12S,15S,16RS) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16 -	9,1
	methyl - prosta - 10,13 - dien - 9 - one.	Ac
55	(5Z) - (8R,12S,15S) - 1 - Methoxyacet-	pn
	oxy - 15 - hydroxy - prosta - 5,10 - dien -	_
	9 - one. (57) - (88 128 158) 1 (2 Corborn	Ca
	(5Z) - (8R,12S,15S) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - prosta - 5,10 -	5,
60	dien - 9 - one.	Ph
	(5Z) - (8R,12S,15R) - 1 - (2 - Carboxy -	9,1
	propionyloxy) - 15 - hydroxy - 16,16 - di-	
	methyl - prosta - 5,10 - dien - 9 - one. (5Z) - 8R,12S,15R,16RS) - 1 - (2 - Carb-	Pb
	() orgino, 12 square, -1 * (2 * Caro-	pr

oxy - propionyloxy) - 15 - hydroxy - 16 - methyl - prosta - 5,10 - dien - 9 - one.	65
(8R,12S,15R) - 1 - (2 - Carboxy - pro- pionyloxy) - 15 - hydroxy - 16,16 - dimethyl -	
prost - 10 - en - 9 - one. (8R,12S,15R,16RS) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16 - methyl -	7 0
prost - 10 - en - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 -	
Carboxy - propionyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien -	7 5
9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy -	
16 - phenoxy - 17,18,19,20 - tetranor - presta - 5,13 - dien - 9 - one.	80
(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor -	
prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 -	85
Carboxy - propionyloxy) - 11,15 - dihydroxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien -	
9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 -	90
Carboxy - propionyloxy) - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.	
(5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy 16 - (4 - chlorophenoxy) - 17,18,19,20 -	95
tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 -	
Carboxy - propionyloxy) - 16 - (3 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.	100
(5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy -	
16 - (3 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 -	105
Carboxy - propionyloxy) - 16 - (4 - fluoro- phenoxy) - 17,18,19,20 - tetranor - prosta -	
5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy -	110
16 - (4 - fluorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 -	
triol. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - prosta - 5,13 - dien -	115
9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15S) - 1 - (N -	
Acetyl - carbamoyloxy) - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,12S,15S) - 1 - (N - Acetyl -	120
carbamoyloxy) - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.	
(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Phenylcarbamoyloxy) - prosta - 5,13 - dien - 9,11,15 - triol.	125
(5Z,13E) - (8R,9S,11R,12R,15S) - (1 - (N - Phenylcarbamoyloxy) - 11,15 - dihydroxy -	
prosta - 5,13 - dien - 9 - one.	

/	1,33.	7,710	
	(5Z,13E) - (8R,12S,15S) - 1 - (N - Phenyl- carbamoyloxy) - 15 - hydroxy - prosta -	tetranor - prosta - 5,13 - dien - 9 - one.	65
5	5,10,13 - trien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Methyl - thiocarbamoyloxy) - prosta - 5,13 -	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 17 - phenyl - 18,19,20 - trinor - prosta - 5,3 - dien	70
	dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methyl - thiocarbamoyloxy) - 11,15 - di-	9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - 17 - phenyl - 18,19,20 - trinor - prosta -	<i>1</i> 0
10	hydroxy - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,12S,15S) - 1 - (N - Methyl- thiocarbamoyloxy) - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.	5,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - 11 -	75
15	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.	methyl - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - methyl - prosta - 5,13 - dien - 9,11,15 -	80
	(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.	triol. (5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy]	
20	(5Z,13E) - (8R,12S,15S) - 1 - (N - Methyl- carbamoyloxy) - 15 - hydroxy - 15 - methyl	11,15 - dihydroxy - 15 - methyl - prosta -	85
	prosta - 5,10,13 - trien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15S,16RS) - 1 - (N - Methylcarbamoyloxy) - 16 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.	Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - 15 - methyl - prosta - 5,10,13 - trien - 9 - one.	
25	(5Z,13E) - (8R,11R,12R,15S,16RS) - 1 - (N - Methylcarbamoyloxy) - 11,15 - di- hydroxy - 16 - methyl - prosta - 5,13 - dien -	(5Z,13E) - (8R,9S,11R,12R,16RS) - 1 - [(N - Methanesulphonyl) - carbamoyloxy] - 16 - methyl - prosta - 5,13 - dien - 9,11,15 -	90
30	9 - one. (5Z,13E) - (8R,12S,15S,16RS) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - 16 - methyl - prosta - 5,10,13 - trien - 9 - one.	triol. (5Z,13E) - (8R,11R,12R,15S,16RS) - [(N Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - 16 - methyl - prosta -	95
35	(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R - 1 - (N -	5,13 - dien - 9 - one. (5Z,13E) - (8R,12S,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - 16 - methyl - prosta - 5,10,13 -	100
	Methylcarbamoyloxy) - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one.	trien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - [(N - Methane - sulphonyl) - carbamoyloxy] - 16,16 - dimethyl - prosta - 5,13 - dien -	
40	(5Z,13E) - (8R,12S,15R) - 1 - (N - Methyl-carbamoyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R - 1 - (N - Methylcarbamoyloxy) - 16 - phenoxy -	9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 16,16 - dimethyl - 11,15 - dihydroxy -	105
45	17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy -	prosta - 5,13 - dien - 9 - one.	110
50	16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N -	trien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 16 -	115
	Methylcarbamoyloxy) - 16 - (3 - trifluoro- methylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - (N	phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - 11,15 - dihydroxy - 16 - phenoxy -	
5 5	methylcarbamoyloxy) - 11,15 - dihydroxy 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien- 9 - one.	17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - [(N Methane - sulphonyl) - carbamoyloxy] - 16 -	120
60	(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13	(3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - [(N -	125
•	dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy -	Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - 16 - (3 - trifluoromethyl-	

	phenoxy) - 17,18,19,20 - tetranor - prosta -	Acetyl - carbamoyloxy) - 16,16 - dimethyl -	
	5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - [(N -	prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E3 - (8R,11R,12R,15R) - 1 - (N -	
5	Methane - sulphonyl) - carbamoyloxy] - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor -	Acetyl - carbamoyloxy) - 16 - phenoxy 9 - one.	70
J	prosta - 5,13 - dien - 9,11,15 - triol.	(5Z,13E) - (8R,12S,15R) - 1 - (N - Acetyl -	70
	(5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] -	carbamoyloxy) - 15 - hydroxy - 16,16 - di- methyl - prosta - 5,10,13 - trien - 9 - one.	
	11,15 - dihydroxy - 16 - (4 - chlorophenoxy) -	(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N -	
10	17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.	Acetyl - carbamoyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien -	75
	(5Z,13E) - (8R,9S,11R,12R,15R) -](N -	9,11,15 - triol.	
	Methane - sulphonyl) - carbamoyloxy] - 16 - (3 - chlorophenoxy) - 17,18,19,20 - tetranor -	(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy -	
15	prosta - 5,13 - dien - 9,11,15 - triol.	16 - phenoxy - 17,18,19,20 - tetranor - prosta -	80
	(5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] -	5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N	
	11,15 - dihydroxy - 16 - (3 - chlorophenoxy) -	Acetyl - carbamoyloxy) - 16 - (3 - trifluoro-	
20	17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.	methylphenoxy) - 17,18,19,20 - tetranor - prosta - 5.13 - dien - 9,11,15 - triol.	85
	(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - [(N -	(5Z,13E) - (8R,11R,12R,15R) - 1 - (N -)	
	Methane - sulphonyl) - carbamoyloxy] - 16 - (4 - fluorophenoxy) - 17,18,19,20 - tetranor -	Acetyl - carbamoyloxy) - 11.15 - dihydroxy - 16 - (3 - trifluoromethylphenoxy) -	
25	prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - [(N -	17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.	00
23	Methane - sulphonyl) - carbamoyloxyl -	(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N -	90
	11,15 - dihydroxy - 16 - (4 - fluorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien -	Acetyl - carbamoyloxy) - 16 - (4 - chloro- phenoxy) - 17,18,19,20 - tetranor - prosta -	
40	9 - one.	5,13 - dien - 9.11,15 - triol.	
30	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 17 -	(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy -	95
	phenyl - 18,19,20 - trinor - prosta - 5,13 -	16 - (4 - chlorophenoxy) - 17,18,19,20 -	
	dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15S) - 1 - [(N -	tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N -	
35	Methane - sulphonyl) - carbamoyloxy - 11,15 - dihydroxy - 17 - phenyl - 18,19,20 -	Acetyl - carbamoyloxy) - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien -	100
	trinor - prosta - 5,13 - dien - 9 - one.	9,11,15 - triol.	
	(5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] -	(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy -	
40	11,15 - dimethyl - 15 - hydroxy - prosta -	17 - phenyl - 18,19,20 - trinor - prosta-	105
	5,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15S) - 1 - [(N -	5,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15S) - 1 - (N -	
	Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - 11 - methyl - prosta - 5,13 - dien -	Acetyl - carbamoyloxy) - 15 - hydroxy - 11 - methyl - prosta - 5,13 - dien - 9 - one.	
45	9 - one.	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N -	110
	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Acetyl - carmaboyloxy) - 15 - methyl -	Phenyl - carbamoyloxy) - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.	
	prosta - 5,13 - dien - 9,11,15 - triol.	(5Z,13E) - (8R,11R,12R,15S) - 1 - (N -	
50	(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy -	Phenyl - carbamoyloxy) - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.	115
	15 - methyl - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,12S,15S) - 1 - (N - Acetyl -	(5Z,13E) - (8R,12S,15S) - 1 - (N - Phenyl -	
	carbamoyloxy) - 15 - hydroxy - 15 - methyl -	carbamoyloxy) - 15 - hydroxy - 15 - methyl - prosta - 5,10,13 - trien - 9 - one.	
55	prosta - 5,10,13 - trien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15S,16RS) - 1 -	(5Z,13E) - (8R,9S,11R,12R,15S,16RS) - 1 - (N - phenyl - carbamoyloxy) - 16 -	120
	(N - Acetyl - carbamoyloxy) - 16 - methyl -	methyl - prosta - 5,13 - dien - 9,11,15 -	
	prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15S,16RS) - 1 -	triol. (5Z,13E) - (8R,11R,12R,15S,16RS) - 1 -	
60	(N - Acetyl - carbamoyloxy) - 11,15 - di- hydroxy - 16 - methyl - prosta - 5,13 - dien -	(N - phenyl - carbamoyloxy) - 11,15 - di-	125
00	9 - one.	hydroxy - 16 - methyl - prosta - 5,13 - dien - 9 - one.	143
	(5Z,13E) - (8R,12S,15S,16RS) - 1 - (N - Acetyl - carbamoyloxy) - 15 - hydroxy - 16 -	(5Z,13E) - (8R,12S,15S,16RS) - 1 - (N - phenyl - carbamoyloxy) - 15 - hydroxy - 16 -	
	methyl - prosta - $5,10,13$ - trien - 9 - one.	methyl - prosta - 5,10,13 - trien - 9 - one.	
65	(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N -	(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N -	130

one. (SZ,13E) - (8R,12S,15R) - 1 - (N - phenyl-carbamoyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one. (SZ,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol. (SZ,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - trinor - prosta - 5,13 - dien - 9 - one. (SZ,13E) - (8R,9S,11R,12R,15S) - 1 - (N - phenyl - carbamoyloxy				_
phenyl - carbamoyloxy) 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,12S,15R) - 1 - (N - phenyl - carbamoyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15S) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15S) - 1 - (N - phenyl - carbamoyloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15S) - 1 - (N - phenyl - carbamoyloxy) - 15 - hydroxy - 15 - hyd		prosta - 5,13 - dien - 9,11,15 - triol.	dien - 9 - one.	
one. (5Z,13E) - (8R,12S,15R) - 1 - (N - phenyl-carbamoyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol. (5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 1,1,15 - dihydroxy - 15 - hydroxy - 16 - methyl - prosta - 5,13 - dien - 9, 11,15 - triol. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 1,1,15 - dihydroxy - 16 - methyl - prosta - 1,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 1,1,15 - dihydroxy - 16 - methyl - prosta - 1,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 1,1,15 - dihydroxy - 16 - methyl - prosta - 1,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 1,1,15 - dihydroxy - 16 - methyl - prosta - 5,13 - dien - 9 - one. (5Z,13E) - (8R,11R,12R,15S) - 1 - (N - phenyl - carbamoyloxy) - 1,1,15 - dihydroxy - 1,1,15 - dihydr	_	phenyl - carbamoyloxy) - 11,15 - dihydroxy -	thiocarbamoyloxy) - 15 - hydroxy - 16,16 -	
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16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prost - 5.13 - dien - 9 - one.		(5Z,13E) - (8R,11R,12R,15R) - 1 - (N -	carbamoyloxy) - 15 - hydroxy - 16 - methyl -	
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16 - methyl - prosta - 5,10,13 - trien - 9 - dimethyl - prosta - 5,13 - dien - 9 - one.		16 - methyl - prosta - 5,10,13 - trien - 9 -	dimethyl - prosta - 5,13 - dien - 9 - one.	
one. 13E) - (8R,11R,12R,15S) - 1 - (N - (5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - 11,15 -				
65 methyl - thiocarbamoyloxy) - 11,15 - di- dimethyl - prost - 13 - en - 9 - one.	65			

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The new esters of prostan - 1 - ol derivatives of the general formula I are valuable pharmacological products, as, while having a similar spectrum of action, they have a considerably stronger and above all considerably longer action than do the corresponding natural prostaglandins.

The new prostaglandin analogues of the E-, D- and F- type have a very strong luteolytic action, that is to say, for causing luteolysis considerably smaller dosages are required than in the case of the corresponding natural prostaglandins.

Also for causing abortions, considerably smaller quantities of the new prostaglandin analogues are required than in the case of the natural prostaglandins. The tests were carried

out on pregnant rats and guinea-pigs by the usual methods. Thus, pregnant rats were treated subcutaneously from the 4th to 7th day of pregnancy with the compounds of the present invention. On the 9th day the animals were killed and the uteri were examined at the places of nidation. As is shown in the following Table with reference to compounds 1 to 7 as examples, the compounds of the present invention in a 3 to 100 times smaller dose have just as good an abortive action as 1 mg per animal of PG F_{2a}. Thus for example, (5Z,13E) - (8R,11R,12R,15R) - 1 - acetoxy - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one, as compared with 1 mg per animal of PG E₂, has just as good an abortive action at a dose 100 times smaller.

Relative action

TABLE

40	1	Tested compound. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - Acetoxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol	(PG F _{2d} =1) on abortion in the rat. 100
45	2	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol	10
50	3	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9,11,15 - triol	5
	4	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - prosta - 5,13 - dien - 9,11,15 - triol	. 3
55	5	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol	3
60	6	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(Methoxy) - acetoxy] - prosta - 5,13 - dien - 9,11,15 - triol	3
	7	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Isobutyryloxy - prosta - 5,13 - dien - 9,11,15 - triol	3

In recording the isotonic uterus contraction of narcotised rats and the isolated rat uterus it is found that the compounds of the present invention are considerably more active and their actions last longer than in the case of the natural prostaglandins.

The new compounds of the present invention are suitable, after a single intrauterine application, for inducing a menstruation or interrupting a pregnancy. It is to be regarded as a therapeutic advance that, in addition to the surprisingly good dissociation of anti-

fertile properties, effects on other organ systems are almost completely prevented. They are also suitable for the synchronisation of the sexual cycle in female mammals, for example apes, rabbits, cattle and pigs.

The good dissociation of action of the compounds of the present invention is shown in the investigation of other unstriated-muscular organs, for example the ileum or guineapigs or the isolated trachea of rabbits, where a considerably smaller stimulation is observed than in the case of the natural prostaglandins.

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(3H,m);

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The active compounds of the PG E-series of the present invention exhibit on the isolated trachea of the rabbit in vitro a bronchodilatory action and strongly check the secretion of gastric acid and have a regulating action in disturbances of cardiac rhythm. The new compounds of the PG A- and PG E-series also lower the blood pressure and have a diuretic action.

The active compounds of the F-series of the present invention have a less bronchoconstrictive action than does natural prostaglanlin F₂₀, which is a great advantage for their therapeutic use. For medicinal use the active substances may be converted into a form suitable for inhalation, or for oral or parenteral application. For inhalation it is of advantage to prepare aerosol or spray solutions.

For oral application there are suitable, for

example, tablets, dragees or capsules.

For parenteral administration there are used sterile, aqueous or oily solutions suitable for injection.

The present invention therefore further provides a pharmaceutical preparation which comprises a compound of the general formula I, in admixture or conjunction with a pharmaceutically suitable carrier. The preparations may contain the usual auxiliary and carrier substances.

The active compounds of the present invention serve in combination with the auxiliary substances known and normally used in galenical pharmacy, for example, for the production of preparations for causing an abortion, for controlling menstruation or for inducing a birth. For these purposes there may be used sterile, aqueous solutions, which contain 0.01 to 10μ grams per ml of active compounds, as an intravenous infusion. The compounds of the general formula I are especially suitable for the preparation of aqueous isotonic solutions. In order to increase solubility there may be added alcohols, for example ethanol, ethylene glycol and propylene glycol.

ethylene glycol and propylene glycol.

The following Examples illustrate the invention:

Example 1
(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - prosta - 5,13 - dien - 9,11,15 - triol.
A mixture of 550 mg of (5Z,13E) (8R,9S,11R,12R,15S) - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 dien - 1 - ol, 2.5 ml of pyridine and 1 ml of
acetic anhydride was allowed to stand for 14
hours at room temperature. The mixture was
evaporated in vacuo, and there were obtained
600 mg of (5Z,13E) - (8R,9S,11R,12R,15S) 1 - acetoxy - 9,11,15 - tris(tetrahydropyran 2 - yloxy) - prosta - 5,13 - diene in the form
of a pale yellow oil.

IR (CHCl₃): 1738, 1240/cm.

The 1-acetate so obtained was stirred for 4 hours at 50°C with 15 ml of a mixture of acetic acid/water/tetrahydrofuran (65/35/10), evaporated in vacuo, and the residue was purified by column chromatography over silica gel. With diethyl ether/ethyl acetate (8+2) 290 mg of the title compound were obtained in the form of a colourless oil.

IR (CHCl₃):

3600, 3430 (wide), 3000, 2930, 2860, 1738, 1240, 972 /cm.

NMR (CDCl₃):

The starting material for the above compound was prepared as follows:

8.05 (3H,s); 0.90 (3H,t,J=7Hz).

δ: 5.3—5.6 (4H,m); (2H,t,J=6,5Hz); 3.85—4.28

(a) Prostaglandin F_{2a} - 9,11,15 - tris(tetrahydropyran - 2 - yl) - ether methyl ester. To a solution of 153 mg of PG F_{2a} methyl ester in 6 ml of methylene chloride were added at 5°C 0.45 ml of dihydropyran and 85 2 mg of para-toluene sulphonic acid, the mixture was stirred for 30 minutes at 0°C, added to 3 ml of a saturated solution of sodium bicarbonate, diluted with diethyl ether, and the organic phase was agitated 90 twice with water, dried over magnesium sulphate and evaporated in vacuo. After filterin the evaporation residue over silica gel, there were obtained with diethyl ether/hexane (1+1) 216 mg of the title compound in the form of a colourless oil.

TLC (diethylether/hexane 7+3): Rf-value 0.75.

(b) (5Z,13E) - (8R,9S,11R,12R,15S) - 9,11,15 - Tris(tetrahydropyran - 2 - 100

yloxy) - prosta - 5,13 - dien - 1 - ol. To a suspension of 500 mg of lithium aluminium hydride in 25 ml of diethylether was added dropwise at 10°C a solution of 1 gram of the compound prepared in accordance with Example 1(a) in 25 ml of diethylether, and the whole was stirred for 1.5 hours at room temperature. The excess of lithium aluminium hydride was then destroyed by the dropwise addition of ethyl acetate, 2 ml of water were added, and the mixture was stirred for 45 minutes at room temperature, filtered and evaporated in vacuo. After filtering the residue over silica gel, there were obtained with hexane/diethylether (3+2) 880 mg of the title compound in the form of a colourless oil.

IR (CHCl₃):
3600, 3430 (wide), 3000, 2938, 2860,
1600, 975 /cm.

NMR (DMSO-d₄:
δ: 5.2—5.55 (4H,m); 4.45—4.73
(3H,m); 4.3 (1,t,J=5Hz); 0.88
(3H,t,J=7Hz).

	Example 2 (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Iso-
	butyryloxy - prosta - 5,13 - dien - 9,11,15 - triol.
5	A mixture of 300 mg of the compound prepared in accordance with Example 1(b),
	prepared in accordance with Example 1(b), 2 ml of pyridine and 0.5 ml of isobutyric acid
	chloride was stirred for 14 hours at room
10	temperature under argon. The mixture was evaporated in vacuo, and there was obtained
10	as a crude product (5Z.13E) - (8R.9S.11R.
	12R,15S) - 1 - isobutyryloxy) - 9.11.15 - trie-
	(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a yellowish oil, which,
15	Without further purification, was stirred with
	7 ml of a mixture of acetic acid/water/tetra- hydrofuran (65/35/10) for 5 hours at 50°C.
	After evaporation and chromatography of the
20	residue over silica gel there were obtained
20	with diethylether/ethyl acetate (8+2) 160 mg of the title compound in the form of a colour-
	less oil.
	IR (CHCl _s):
٥.	3600, 3430 (wide), 2938, 2860, 1725,
25	1160, 973 /cm. NMR (CRCl ₂):
	8. 523-556 (ALT-1), 405
	(2H,t,J=7Hz); 3.8—4.46 (3H,m); 1.16 (6H,d,J=7Hz); 0.90 (3H,t,J=6.5Hz).
20	•
30	Example 3 (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - benzoyl-
	oxy - prosta - 5,13 - dien - 9,11,15 - triol. A mixture of 500 mg of the compound pre-
	pared in accordance with Example 1/h) 7 ml
3 5	of pyridine and 0.5 ml of henzovi chloride was
	stirred for 14 hours at room temperature under argon. Then there were added 5 ml of
	water, the mixture was stirred for 2 hours at
40	room temperature, extracted three times with diethylether, and the organic extract was
10	agitated twice with a saturated solution of
	sodium bicarbonate, twice with water, dried over magnesium sulphate and evaporated in
	vacuo. There were obtained 545 mg of
45	$(5Z_013E) = (8R.9S.11R.12R.15S) = 1 = hentovil$
	oxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form
	of a colouriess of that was completely unitary
	according to thin-layer chromatography.
50	TLC (diethylether/hexane 7+3):
	Rf-value 0.78.
	The 1 - benzoate so obtained was stirred for 5 hours at 50°C with 15 ml of a mixture
	of glacial acetic acid/water/tetrahydrofuses
55	of glacial acetic acid/water/tetrahydrofuran (65/35/10), evaporated in vacuo, and the residue was purified by preparative layer chromatography over silica gel plates with diethylether/dioxane (7+3) as antening
	residue was purified by preparative layer
	diethylether/dioyane (7-13) as asserting

agent. There were obtained 245 mg of the

title compound in the form of colourless cry-

stals. Melting point 42°C.

TLC (diethylether/dioxane 8+2): Rf-value 0.27. IR (CHCl₃) 3600, 3420, (wide), 3000, 2938, 2860, 65 1710, 1600, 1278, 970 /cm. NMR (CDCI₃): δ: 7.4—7.6 (3H,m); 7.93—8.09 (2H,m); 5.25—5.58 (4H,m); 4.31 (2H,t,J=7Hz); 0.90 (3H,t,J=7Hz). 70 Example 4 (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Butyryloxy - prosta - 5,13 - dien - 9,11,15 - triol. A mixture of 300 mg of the compound prepared in accordance with Example 1(b), 2 75 ml of pyridine and 0.5 ml of butyric anhydride was allowed to stand for 14 hours at room temperature. By evaporation there was obtained in the form of a crude product (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - butyryl-80 oxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a pale yellow oil, which, without further purification, was stirred with 7 ml of a mixture of glacial acetic acid/water/tetrahydrofuran 85 (65/35/10) for 4 hours at 50°C. By evaporation and chromatography of the residue over silica gel there were obtained with diethyl-ether/ethyl acetate (8+2) 172 mg of the title compound in the form of a colourless oil. 90 IR (CHCl₃): 3600, 3430 (wide), 3000, 2930, 2860, 1737, 972 /cm. Example 5 (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Deca-95 noyloxy - prosta - 5,13 - dien - 9,11,15 triol. A mixture of 200 mg of the compound prepared in accordance with Example 1(b), 1.4 ml of pyridine and 0.4 ml of decanoic 100 acid chloride was allowed to stand for 14 hours at room temperature, 0.2 ml of water was added, and the mixture was allowed to stand for a further 2 hours, diluted with 50 ml of water and extracted three times with 30 ml of diethylether each time, and the organic phase was agitated in succession with a saturated solution of sodium bicarbonate and brine, dried over magnesium sulphate and evaporated to dryness in vacuo. The (5Z,13E) -(8R,9S,11R,12R,15S) - 1 - decanoyloxy 9,11,15 - tris(tetrahydropyran - 2 - yloxy) prosta - 5,13 - diene so obtained was stirred with 5 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) for 5 hours 115 at 50°C. After evaporating, chromatography was carried out over silica gel with diethylether/ethyl acetate (9+1), and 150 mg of the title compound were obtained in the form of a colourless oil. 120 IR (CHCl₃):

3600, 3430 (wide), 2930, 2860, 1730,

970 /cm.

	:EI- (The starting meterial for the shows are	
	Example 6 (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [Methoxy) - acetoxy] - prosta - 5,13 - dien -	The starting material for the above compound was prepared as follows:	
5	9,11,15 - triol. A mixture of 310 mg of the compound	(a) (5Z,13E) - (8R,9S,11R,12R,15S) - 9,11,15 - Tris(tetrahydropyran - 2 -	65
,	prepared in accordance with Example 1(b), 2 ml of pyridine and 0.5 ml of methoxy - acetic acid chloride was stirred for 13 hours	yloxy) - prosta - 5,13 - dien - 1 - ol. To a solution, cooled to -65°C of 1.68 grams of the compound prepared in accord-	
10	at room temperature under argon. The mix- ture was evapoated in vacuo, and there was obtained as a crude product (5Z,13E) -	ance with Example 1(a) in 80 ml of toluene were added dropwise 12 ml of a solution of 20% strength of diisobutyl - aluminium	70
	(8R,9S,11R,12R,15S) - 1 - [(methoxy) - acet- oxy] - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form	hydride in toluene, the mixture was stirred for 15 minutes at =65°C, the excess of reagent was decomposed by the dropwise addi-	
15	of a yellowish oil, which, without further purification, was stirred with 7 ml of a mix- ture of glacial acetic acid/water/tetrahydro-	tion of isopropanol, 6 ml of water were added, the mixture was allowed to warm up to 5°C, stirred for one hour, the precipitate was	75
20	furan (65/35/10) for 5 hours at 48°C. By evaporation and chromatography of the resi-	filtered off, and the filtrate was evaporated to dryness in vacuo. There were obtained 1.68	90
20	due over silica gel there were obtained with diethylether/ethyl acetate (7+3) 158 mg of the title compound in the form of a colourless	grams of the title compound in the form of a colourless oil.	80
	oil.	TLC (diethylether/hexane 7+3): Rf-value 0.68	
25	IR (CHCl ₂): 3600, 3435 (wide), 3000, 2930, 2865.	IR (CHCl ₃): 3000, 2942, 2860, 2730, 1721, 968 /cm.	0.6
	1740, 975 /cm.	NMR (DMSO- d_a):	85
	Example 7	δ: 9.63 (1H,t,J=2Hz); 5.15—5.55 (4H,m); 4.38—4.73 (3H,m); 0.85	
	(5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1 -	(3H,t,J=6,5Hz).	
30	Acetoxy - 1 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.	(b) (5Z,13E) - (1RS,8R,9S,11R,12R,15S) -	90
	A mixture of 700 mg of (5Z,13E) -	1 - Methyl - 9,11,15 - tris(tetrahydro-	
	(1RS,8R,9S,11R,12R,15S) - methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta -	pyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol.	
35	5,13 - dien - 1 - ol, 3.7 ml of pyridine and 1.5 ml of acetic anhydride was allowed to	To a solution of 1.68 grams of the aldehyde prepared in accordance with Example 7(a) in	95
	stand for 14 hours at room temperature. The	57 ml of diethylether and 57 ml of tetrahydro-	
	mixture was evaporated in vacuo, and 770 mg of (5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1 -	furan were added at 0°C under argon 2.84 ml of an approximately 2-molar solution of	
40	acetoxy - 1 - methyl - 9,11,15 - tris(tetrahydro-	lithium methyl in diethylether, the mixture	100
40	pyran - 2 - yloxy) - prosta - 5,13 - diene, which was unitary according to thin-layer	was stirred for 20 minutes at 0°C, 50 ml of a saturated solution of ammonium chloride	100
	chromatography, were obtained in the form of	were added, extraction was carried out three	
	a colourless oil.	times with diethylether, and the organic ex- tract was agitated twice with water, dried over	.05
45	TLC (diethylether/hexane 7+3): Rf-value 0.73.	magnesium sulphate and evaporated in vacuo. There were obtained 1.61 grams of the title	105
	IR (CHCl _s):	compound in the form of a colourless oil.	
	3000 2940, 2860, 1727, 1255, 978 /cm. The 1 - acetate so obtained was stirred for	TLC (diethylether/hexane 7+3):	
	14 hours at room temperature with 20 ml	Rf-value 0.24.	110
50	of a mixture of glacial acetic acid/water/ tetrahydrofuran (65/35/10), evaporated in	IR: 3600, 3450, 3000, 2940, 2860, 978 /cm.	110
	vacuo, and the residue was purified by column	Example 8	
	chromatography over silica gel. With diethylether/ethyl acetate (8+2) were obtained 385	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acet-	
55	mg of the title compound in the form of a	oxy - 1,1 - 1,1 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol.	115
	colourless oil.	A solution of 980 mg of (5Z,13E) -	
	TLC (diethylether/dioxane 8+2): Rf-value 0.29.	(8R,9S,11R,12R,15S) - 1,1 - dimethyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) -	
د ۸	IR (CHCl ₃):	prosta - 5,13 - dien - 1 - ol in 30 ml of	120
60	3600, 3430, wide, 3000, 2930, 2860, 1727, 1255, 978 /cm.	methylene chloride was mixed with 296 mg of 4 - dimethylaminopyridine and 2.3 ml of	

5	acetic anhydride, and the whole was allowed to stand for 4 days at room temperature. After evaporation in vacuo, the residue was filtered with hexane/diethylether (1+1) over silica gel, and there were obtained 985 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - acetoxy - 1,1 - dimethyl - 9,11,15 - tris(tetrahydropyran - 2 - xyloxy) - prosta - 5,13 - diene in the form of a colourless oil.	5,13 - dien - 1 - ol, 2 ml of pyridine and 0.5 ml of acetic anhydride was allowed to stand for 14 hours at room temperature. The mixture was evaporated in vacuo, and there was obtained as a crude product (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - acetoxy - 15 methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a yellowish oil.	60
10	TLC (diethylether/hexane 7+3): Rf-value 0.75.	IR (CHCl ₃): 1738, 1240, 975 /cm.	70
16	IR (CHCl ₃): 3000, 2940, 2860, 1723, 1260, 978 /cm.	The 1 - acetate so obtained was stirred for 14 hours at room temperature with 8 ml of a mixture of glacial acetic acid/water/tetra-hydrofuran (65/35/10), the mixture was	7.6
15	The 1 - acetate so obtained was stirred for 14 hours at 25°C with 18 ml of a mixture of acetic acid/water/tetrahydrofuran (65/35/10), evaporated in vacuo, and the residue was purified by column chromatography over silica	evaporated in vacuo, and the residue was purified by chromatography over silica gel. With diethylether/ethyl acetate (8+2) were obtained 152 mg of the title compound in the form of a colourless oil.	75
20	gel. With diethylether/ethyl acetate (8+2) there were obtained 380 mg of the title compound in the form of a colourless oil.	IR: 3595, 3430 (wide), 3000, 2935, 2860, 1738, 1240, 975 /cm.	80
25	IR (CHCl ₃): 3600, 3440 (wide), 3000, 2935, 2860, 1724, 1260, 978 /cm. NMR (CDCl ₃):	The starting material for the above compound was prepared as follows:	
	8: 5.2—5.6 (4H,m); 3.8—4.3 (3H,m); 1.98 (3H,s); 1.42 (6H,s); 0.88 (3H,t,J=7Hz).	 (a) (15S) - 15 - Methyl - prostaglandin F_{2α} - 9,11,15 - tris(tetrahydropyran - 2 - yl) - ether methyl ester. 	85
30	The starting material for the above compound was prepared as follows:	To a solution of 160 mg of (15S) - 15 - methyl - PG $F_{2\alpha}$ - methyl ester [Journal of the American Chemical Society, 96 (18), 5865 (1974)] in 6 ml of methylene chloride were	90
35	(a) (5Z,13E) - (8R,9S,11R,12R,15S) - 1,1 - Dimethyl - 9,11,15 - tris - (tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol.	added at 5°C 0.5 ml of dihydropyran (freshly distilled) and 2 mg of para-toluene sulphonic acid, the mixture was stirred for 30 minutes	95
33	To a solution of 1.47 grams of the compound prepared in accordance with Example 1(a) in 48 ml of diethylether and 48 ml of	at 5°C, added to 4 ml of a saturated solution of sodium bicarbonate, diluted with diethyl- ether, and the organic phase was agitated twice with water, dried over magnesium sul-	93
40	tetrahydrofuran were added at 0°C under argon 7 ml of a 2-molar solution of lithium methyl in diethylether. After 20 minutes the mixture was diluted with diethylether, agitated with a saturated solution of sodium chloride,	phate and evaporated <i>in vacuo</i> . After filtering the evaporation residue over silica gel there were obtained with diethylether/hexane (1+1) 210 mg of the title compound in the form of a colourless oil.	100
45	dried with magnesium sulphate, and evaporated in vacuo. There were obtained 1.53 grams of the tile compound in the form of a colourless oil. TLC (diethylether/hexane 7+3):	TLC (diethylether/hexane 7+3): Rf-value 0.78. IR (CDCl ₃): 1736, 975 /cm.	105
50	Rf-value 0.31 IR (CHCl ₃): 3600, 3430 (wide), 3000, 2940, 2860, 978 /cm.	(b) (5Z,13E) - (8R,9S,11R,12R,15S) - 15 - Methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol. To a suspension of 100 mg of lithium alumi-	110
55	Example 9 (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol. A mixture of 310 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 15 - methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta -	nium hydride in 5 ml of diethylether was added dropwise at 5°C a solution of 0.2 gram of the compound prepared in accordance with Example 9(a) in 5 ml of diethylether, and the whole was stirred for 2 hours at 22°C. The excess of lithium aluminium hydride was then decomposed by the dropwise	115

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addition of ethyl acetate, 0.5 ml of water was added, and the mixture was stirred for 40 minutes at room temperature, filtered and evaporated in vacuo. By filtration of the residue over silica gel there were obtained with hexane/diethylether (3+2) 177 mg of the title compound in the form of a colourless oil. IR (CHCl₃): 3600, 3430 (wide), 2998, 2940, 2860.

976 /cm.

Example 10 (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - Acetoxy - 16 - phenoxy - 17,18,19,20 - tetranor prosta - 5,13 - dien - 9,11,15 - triol.

mixture of 195 mg of (5Z,13E) (8R,9S,11R,12R,15R) - 16 - phenoxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) -17,18,19,20 - tetranor - prosta - 5,13 - dien - 1 - ol, 1 ml of pyridine and 0.5 ml of acetic anhydride was allowed to stand for 14 hours at room temperature. The mixture was evaporated in vacuo, and there were obtained 206 mg of (5Z,13E) - (8R,9S,11R,12R,15R) -1 - acetoxy - 16 - phenoxy - 9,11,15 - tris-(tetrahydropyran - 2 - yloxy) - 17,18,19,20 tetranor - prosta - 5,13 - diene in the form of a colourless oil.

IR (CHCl₃): 3000, 2936, 2860, 1728, 1600, 1588, 30 1495, 1240, 973 /cm.

> The 1 - acetate so obtained was stirred for 14 hours at room temperature with 8 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10), the mixture was evaporated in vacuo, and the residue was purified by layer chromatography over silica gel plates. With diethylether/dioxane (8+2) there were obtained 72 mg of the title compound in the form of a colourless oil.

40 IR (CHCl₃): 3440, 3000, 2940, 2860, 1728, 1600, 1588, 1495, 1240, 975 /cm.

> The starting material for the above compound was prepared as follows:

(a) (5Z,13E) - (8R,9S,11R,12R,15R) - 16 -45 Phenoxy - 9,11,15 - tris(tetrahydro-pyran - 2 - yloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dienoic acid methyl ester.

To a solution of 140 mg of (5Z,13E) - (8R,9S,11R,12R,15R) - 16 - phenoxy - 9,11,15 - trihydroxy - 17,18,19,20 - tetranor - prosta - dienoic acid methyl ester (see German Offenlegungsschriften 2,223,365 and

2,322,673) in 4.5 ml of methylene chloride were added at 5°C 0.14 ml of dihydropyran and 1.5 mg of para - toluene sulphonic acid, the mixture was stirred for 30 minutes at

5°C, added to 4 ml of a saturated solution of sodium bicarbonate, diluted with diethylether, and the organic phase was agitated twice with water, dried over magnesium sulphate and evaporated in vacuo. After filtration of the residue over silica gel there were obtained with diethylether/hexane (1+1) 205 mg of the title compound in the form of a colourless oil.

TLC (diethylether/hexane 7+3): Rf-value 0.71.

(b) (5Z,13E) - (8R,9S,11R,12R,15R) - 16 - Phenoxy - 9,11 - tris(tetrahydropyran -2 - yloxy) - 17,18,19,20 - tetranor prosta - 5,13 - dien - 1 - ol.

To a suspension of 122 mg of lithium aluminium hydride in 7 ml of diethylether was added dropwise at 5°C a solution of 238 mg of the compound prepared in accordance with Example 10(a) in 7 ml of diethylether, and the whole was stirred for 2 hours at room temperature. The excess of reagent was then decomposed by the dropwise addition of ethyl acetate, 0.8 ml of water was added, and the mixture was stirred for 40 minutes at room temperature, filtered and evaporated in vacuo. After filtration of the residue over silica gel there were obtained with diethylether/hexane (3+2) 196 mg of the title compound in the form of a colourless oil.

IR (CHCl₃): 3600, 3430, 3000, 2940, 2860, 1600. 1588, 1495, 975 /cm.

Example 11 By proceeding as in Example 10, but with the use of (5Z,13E) - (8R,9S,1R,12R,15R) -16 - (3 - trifluoromethylphenoxy) - 9,11,15 trihydroxy - 17,18,19,20 - tetranor - prosta - 5,13 - dienoic acid methyl ester (see German Offenlegungsschriften 2,223,365 and 100 2,322,673), there was obtained (5Z,13E) -(8R,9S,11R,12R,15R) - 1 - acetoxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetra-

in the form of a colourless oil. 105 IR (CHCl₃): 3600, 3430, 3000, 2940, 2860, 1730, 1600, 1592, 1490, 1240, 975 /cm.

nor - prosta - 5,13 - dien - 9,11,15 - triol

Example 12 By proceeding in accordance with Example but with the use of (5Z,13E) -110 (8R,9S,11R,12R,15R) - 16 - (4 - chlorophenoxy) - 9,11,15 - trihydroxy - 17,18,19,20 tetranor - prosta - 5,13 - dienoic acid methyl ester (see German Offenlegungsschriften 2,223,365 and 2,322,673), there was obtained (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - acetoxy - 16 - (4 - chlorophenoxy) - 17,18,19,20 -

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tetranor - prosta - 5,13 - dien - 9,11,15 - triol in the form of a colourless oil.

IR (CHCl₃):
3600, 3430 (wide), 3000, 2950, 2860,
1730, 1600, 1583, 1492, 1245, 975, 872,
828 /cm.

Example 13

By proceeding in accordance with Example 10, but with the use of (5Z,13E) - (8R,9S,11R,12R,15S) - 17 - phenyl - 9,11,15 - trihydroxy - 18,19,20 - trinor - prosta - 5,13 - dienoic acid methyl ester (German Offenlegungsschrift 2,234,709), there was obtained (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - acetoxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9,11,15 - triol in the form of a colourless oil.

IR (CHCl₃): 3600, 3400 (wide), 3000, 2960, 1860, 1732, 1600, 1250, 975 /cm.

Example 14

By proceeding in accordance with Example 10, but with the use of (5Z,13E) - (8R,9S,11R,12R,15S) - 9,15 - dihydroxy - 25 11 - methyl - prosta - 5,13 - dienoic acid methyl ester (see Chemistry and Industry 1973, 635), there was obtained (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - acetoxy - 11 - methyl - prosta - 5,13 - dien - 9,15 - diol in the form of a colourless oil.

IR (CHCl₃):
3600, 3430 (wide), 3000, 2950, 2860,
1725, 1260, 978 /cm.

Example 15

By proceeding in accordance with Example 10, but with the use of (5Z,13E) - (8R,9S,11R,12R,15R) - 16,16 - dimethyl - 9,11,15 - trihydroxy - prosta - 5,13 - dienoic acid methyl ester (see German Offenlegungsschrift 2,221,301), there was obtained (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - acetoxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol in the form of a colourless oil.

IR (CHCl₃):
3600, 3430 (wide), 3000, 2940, 2860,
1730, 1255, 978 /cm.

Example 16 (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy -11,15 - dihydroxy - prosta - 5,13 - dien -9 - one.

To a solution of 93 mg of the 1-acetate prepared in accordance with Example 1 in 4 ml of obsolute acetone were added at -45°C 1.2 ml of N,N - diethyl - trimethylsilylamine, and the whole was stirred for 6.5 hours at -40°C. The mixture was then diluted with 30 ml of diethylether, which had previously

been cooled to -70°C, the mixture was agitated once with 5 ml of an ice-cooled solution of sodium bicarbonate and twice with 5 ml of a saturated solution of sodium chloride each time, dried with sodium sulphate and evaporated in vacuo. The 11,15 - bis(trimethylsilyl ether) obtained in this manner was dissolved in 16 ml of absolute methylene chloride, and a solution of 665 mg of Collins reagent (for preparation see Org. Syntheses Vol. 52, 5) was added at +5°C, and the mixture was stirred for 10 minutes, diluted with 50 ml of diethylether, filtered and evaporated in vacuo. In order to split off the silyl ether protecting groups the residue was stirred with a mixture of 9 ml of methanol, 0.9 ml of water and 0.45 ml of glacial acetic acid for 45 minutes at room temperature. The mixture was then diluted with 60 ml of diethylether, agitated with 10 ml of sodium bicarbonate solution, twice with 10 ml of a saturated solution of sodium chloride each time, dried over magnesium sulphate and evaporated in vacuo. After purification by preparative layer chromatography (diethylether/dioxane 9+1 as entraining agent) over silica gel plates there were obtained 55 mg of the title compound in the form of a colourless oil.

TLC (diethylether/dioxane 9+1): Rf-value 0.35.

IR (CHCl₃):
3600, 3400 (wide), 2998, 2960, 2930,
2860, 1738, 1730, 1602, 973 /cm.

NMR (CDCl₃):
δ: 5.50—5.68 (2H,m); 5.22—5.44
(2H,m); 4.03 (2H,t,J=7Hz); 3.93—4.18
(1H,m); 3,62—3.82 (1H,m); 2.05 (3H,s);
0.90 (3H,t,J=7Hz).

Example 17 (5Z,13E) - (8R,11R,12R,15S) - 1 - Isobutyryloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - isobutyrate prepared in accordance with Example 2 the title compound in the form of a colourless oil.

IR (CHCl₃): 3600, 3430 (wide), 2998, 2938, 2860, 1740, 1725, 1160, 975 /cm.

Example 18
(5Z,13E) - (8R,11R,12R,15S) - 1 - Benzoyl- 110
oxy - 11,15 - dihydroxy - prosta - 5,13 dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - benzoate prepared in accordance with Example 3 the title compound in the form of a colourless oil.

	IR (CHCl ₃): 3600, 3425 (wide), 3000, 2940, 2860, 1740, 1712, 1600, 1278, 973 /cm.	16 there was obtained from the 1,1 - dimethyl - 1 - acetate prepared in accordance with Example 8 the title compound in the form of a colourless oil.	60
5	Example 19 (5Z,13E) - (8R,11R,12R,15S) - 1 - Decanoyloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one. In a manner analogous to that in Example	IR (CHCl ₃): 3595, 3410 (wide), 2960, 2930, 2860, 1738, 1720, 1600, 1265, 970 /cm.	
10	16 there was obtained from the 1 - decanoate prepared in accordance with Example 5 the title compound in the form of a colourless oil.	Example 24 (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.	65
15	IR (CHCl ₃): 3600, 3430 (wide), 3000, 2930, 2860, 1738, 1730, 970 /cm.	In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 9 the title compound in the form of a colourless oil.	70
20	Example 20 (5Z,13E) - (8R,11R,12R,15S) - 1 - Butyryloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.	IR (CHCl ₂): 3600, 3430 (wide), 2930, 2860, 1738 (wide), 1245, 975 /cm.	75
	In a manner analogous to that in Example 16 there was obtained from the 1 - butyrate prepared in accordance with Example 4 the title compound in the form of a colourless oil.	Example 25 (5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien -	
25	IR (CHCl ₃): 3600, 3430 (wide), 300, 2930, 2960, 1738 (wide), 974 /cm.	9 - one. In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 10 the title compound in the form of a colourless	80
30	Example 21 (5Z,13E) - (8R,11R,12R,15S) - 1 - [(Methoxy) - acetoxy] - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.	oil. IR (CHCl ₃): 3600, 3440 (wide), 2940, 2860, 1738, 1728, 1600, 1588, 1495, 1240, 975 /cm.	85
35	In a manner analogous to that in Example 16 there was obtained from the 1 - methoxy-acetate prepared in accordance with Example 6 the title compound in the form of a colourless oil.	Example 26 (5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - (3 - trifluoromethyl- phenoxy) - 17,18,19,20 - tetranor - prosta -	90
	IR (CHCl ₃): 3600, 3440 (wide), 3000, 2933, 2865, 1740 (wide), 975 /cm.	5,13 - dien - 9 - one. In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 11, the title compound in the form of a colourless	95
40	Example 22 (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 1 - methyl - prosta - 5,13 - dien - 9 - one.	oil. IR (CHCl ₃): 3600, 3430 (wide), 3000, 2940, 2860, 1738, 1730, 1600, 1595, 1490, 1240,	100
45	In a manner analogous to that in Example 16 there was obtained from the 1 - methyl - 1 - acetate prepared in accordance with Example 7 the title compound in the form of a colourless oil.	975 /cm. Example 27 (5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien -	105
50	IR (CHCl ₃): 3600, 3430 (wide), 3000, 2930, 2860, 1738, 1727, 1255, 978 /cm.	9 - one. In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 12 the title compound in the form of a colourless oil.	110
55	Example 23 (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 1,1 - dimethyl - prosta - 5,13 - dien - 9 - one. In a manner analogous to that in Example	IR (CHCl ₁): 3600, 3430 (wide), 3000, 2945, 2860, 1738, 1730, 1600, 1583, 1492, 1245 976, 875, 830 /cm.	115

5	Example 28 (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9 - one. In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 13 the title compound in the form of a colourless oil.	prepared in accordance with Example 24 with 8 ml of aqueous acetic acid of 90% strength was stirred for 16 hours at 60°C. The mixture was then evaporated in vacuo, and the residue was purified by preparative layer chromatography (diethylether) over silica gel plates. There were obtained 60 mg of the title compound in the form of a colourless oil.	60
10	IR (CHCl ₃): 3600, 3400 (wide), 3000, 2960, 2860, 1738, 1731, 1600, 1250, 975 /cm.	IR (CHCl ₃): 3600, 3450 (wide), 3000, 2960, 2935, 2860, 1735, 1702, 1240, 974 /cm.	
15	Example 29 (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 15 - hydroxy - 11 - methyl - prosta - 5.13 - dien - 9 - one. In a manner analogous to that in Example	Example 33 (5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1,9,11,15 - Tetracetoxy - 1 - methyl - prosta - 5,13 - diene. A mixture of 530 mg of (5Z,13E) -	70
	16 there was obtained from the 1 - acetate prepared in accordance with Example 14 the title compound in the form of a colourless oil.	(1RS,8R,9S,11R,12R,15S) - 1 - methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol (for preparation	7 5
20	IR (CHCl ₃): 3600, 3430 (wide), 3000, 2950, 2860, 1738, 1725, 1260, 978 /cm.	see Example 7(b)) and 20 ml of a mixture of acetic acid/water/tetrahydrofuran (65/35/10) were stirred for 14 hours at room temperature under argon. The mixture was then evaporated in vacuo, and the residue was puri-	80
25	Example 30 (5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one.	fied by chromatography over silica gel. With diethylether/isopropanol (9+1) were obtained 210 mg of (5Z,13E) - (1RS,8R,9S,11R,12R, 15S) - 1,9,11,15 - tetrahydroxy - 1 - methyl -	85
30	In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 15 the title compound in the form of a colourless oil.	prosta - 5,13 - diene in the form of a colour- less oil. TLC (diethylether/dioxane 7+3):	
	IR (CHCl ₃): 3600, 3420, (wide), 2940, 2860, 1738, 1730, 1255, 975 /cm.	O.21. The tetrol prepared in this manner was allowed to stand at room temperature for	90
35	Example 31 (5Z,13E) - (8R,12S,15S) - 1 - Acetoxy - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one. A mixture of 100 mg of the 1 - acetate prepared accordance with Example 16 with	14 hours with a mixture of 0.2 ml of acetic anhydride and 0.8 ml of pyridine. After evaporation, the tetra - acetate was purified by filtration over silica gel. With diethylether/hexane (8+2) were obtained 280 mg of the title compound in the form of a colourless oil.	95
40	8 ml of an aqueous acetic acid of 90% strength was stirred for 14 hours at 60°C. The mixture was then evaporated in vacuo, and the residue was purified by preparative layer chromatography (diethylether) over silica gel	IR (CHCl ₃): 3000, 2960, 2935, 2860, 1735, 1240, 975 /cm.	100
45	plates. There were obtained 68 mg of the title compound in the form of a colourless oil.	Example 34 (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 -	
50	IR (CHCl ₃): 3600, 3460 (wide), 3000, 2960, 2935, 2860, 1735, 1702, 1240, 970 /cm. NMR (DCl ₃): 3: 7.45 (1H,dd,J=6+2,5Hz); 6.13 (1H,dd,J=6+2Hz); 4.08 (2H,t,J=6.5 Hz); 8.05 (3H,s); 0.90 (3H,t,J=6.5Hz).	Carboxy - propionyloxy) - 16,16 - dimethyl prosta - 5,13 - dien - 9,11,15 - triol. 200 mg of (5Z,13E) - (8R,9S,11R,12R,15R)- 1 - (2 - carboxy - propionyl) - 16,16 - dimethyl - 9 - tribenzylsilyloxy - 11,15 - bis'tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien in 10 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) were stirred for 14 hours at room temperatue,	105
55	Example 32 (5Z,13E) - (8R,12S,15S) - 1 - Acetoxy - 15 - hydroxy - 15 - methyl - prosta - 5,10,13 - trien - 9 - one. A mixture of 95 mg of the 1 - acetate	the mixture was evaporated in vacuo, and the residue was purified by column chromatography over silica gel. With methyl chloride/isopropanol (7+3) were obtained 72 mg of	

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the	title	compound	in	the	form	of	a	colour-
less	oil.	-						

IR (CHCl₃): 3600, 2940, 1728, 976 /cm.

The starting material for the above reaction was prepared as follows:

3.6 Grams of 16,16 - dimethyl - prostaglandin $F_{2\alpha}$ methyl ester - 11,15 - bis(tetrahydropyranyl) ether (prepared in accordance with German Offenlegungsschrift 2,221,301 from the acid with diazomethane) dissolved in 54 ml of pyridine were mixed with 2.82 grams of tribenzylsilyl chloride, and the whole was stirred for 3 hours at 48°C under argon. The solvent was distilled off in vacuo at 15 Torr, and the residue was chromatographed over silica gel. With diethylether/pentane mixtures 4.2 grams of the corresponding 9 - tribenzylsilyl ether were eluted in the form of

20 a colourless oil.

To 4.2 grams of the silyl ether in 180 ml of absolute diethylether were added at 20°C in portions 1.20 grams of lithium aluminium hydride, the mixture was stirred for 3 hours at 20°C, the excess of reagent was decomposed by the dropwise addition of ethyl acetate, 2.8 ml of water were added, and the mixture was stirred for one hour, filtered and evaporated in vacuo. 830 mg of the 1 - alcohol so obtained were dissolved in 1.5 ml of pyridine, 120 mg of succinic anhydride were added, and the whole was stirred for 16 hours at 20°C. 10 ml of water were then added, the mixture was stirred for 15 minutes, extracted with diethylether, and the extract was agitated with brine, dried over magnesium sulphate and evaporated to dryness in vacuo. By

filtration over silica gel with methylene chloride were obtained 530 mg of (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy propionyl) - 16,16 - dimethyl - 9 - tribenzyl-silyloxy - 11,15 - bis(tetrahydropyran - 2 yloxy) - prosta - 5,13 - diene in the form of a colourless oil.

45 IR (CHCl₃): 2940, 1728, 1600, 1495, 1165, 1020, 978 /cm.

Example 35 (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien -50 9 - one.

265 mg of (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16,16 dimethyl - 11,15 - bis(tetrahydropyran - 2 yloxy) - prosta - 5,13 - dien - 9 - one were stirred with 7 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) for 5 hours at 40°C, and then the mixture was evaporated to dryness in vacuo. The oily residue was purified by chromatography over silica gel. With methylene chloride/isopro-

panol (8+2) there were obtained 90 mg of the title compound in the form of a colourless

IR (CHCl₃): 3600, 2940, 1738 (shoulder), 1728, 978 /cm.

The starting material was prepared as follows:

750 mg of (5Z,13E) - (8R,9S,11R,12R,15R)-1 - (2 - carboxy - propionyloxy) - 16,16 - dimethyl - 9 - tribenzylsilyloxy - 11,15 - bis-(tetrahydropyran - 2 - yloxy) - prosta - 5,13 diene and 223 mg of tetrabutyl - ammonium fluoride were stirred in 60 ml of tetrahydrofuran for 2 hours at 0°C, the mixture was diluted with water, acidified with citric acid of 10% strength to a pH-value of 5, extracted with diethylether, and the organic extract was agitated with brine, dried over magnesium sulphate and evaporated to dryness in vacuo. By filtration over silica gel with diethylether there were obtained 430 mg of the 9 - hydroxy compound in the form of a colourless oil.

IR (CHCl₃): 3500 (wide), 2940, 1728, 1468, 1452, 1440, 1125, 1020, 978 /cm.

300 mg of the 9 - hydroxy - compound obtained above were dissolved in 7 ml of acetone and 0.25 ml of Jones reagent was added dropwise at -20°C. After 25 minutes the excess of reagent was decomposed by the addition of isopropanol, and the mixture was diluted with diethylether and agitated until neutral with brine. By drying over magnesium sulphate and evaporation there were obtained 270 mg of the 9 - keto - compound in the form of a colourless oil.

IR (CHCl₃): 100 3600 (wide), 2940, 1738 (shoulder), 1730, 978 /cm.

Example 36 (5Z,13E) - (8R,12R,15R) - 1 - (2 - Carboxy propionyloxy) - 15 - hydroxy - 16,16 - di-

methyl - prosta - 5,10,13 - trien - 9 - one. A mixture of 200 mg of (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - carboxy - propionyloxy) - 11,15 - dihydroxy - 16,16 dimethyl - prosta - 5,13 - dien - 9 - one and 15 ml of acetic acid of 90% strength was stirred for 16 hours at 60°C. The mixture was then evaporated in vacuo, and the residue was purified by preparative layer chromatography (silica gel, methylene chloride/isopropanol 9+1). There were obtained 105 mg of the title compound in the form of a colourless oil.

IR (CHCl₃): 3600, 3500 (wide), 2940, 1730, 1602, 120 976 /cm.

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less oil.

(b) To 2.05 grams of silyl ether in 80 ml

20 Example 37 of absolute diethylether was added in 60 (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N portions at room temperature 0.5 gram Methylcarbamoyloxy) - prosta - 5,13 - dien - 9,11,15 - triol. of lithium aluminium hydride, and the mixture was stirred for 2 hours at 20°C To a solution of 300 mg of the 1 - alcohol 5 the excess of reagent was decomposed obtained in accordance with Example 37(b) with ethyl acetate, 1.2 ml of water were 65 in 5 ml of absolute tetrahydrofuran were added in succession 1.2 ml of methyl isoadded, and the mixture was stirred for one hour at 20°C, filtered and evaporcyanate and 3 drops of triethylamine, the mixated in vacuo. There were obtained 1.95 grams of (5Z,13E) - (8R,9S,11R, 10 ture was allowed to stand overnight at room temperature, evaporated to dryness in vacuo, 12R,15S) - 11,15 - bis(tetrahydro-70 and the residue was purified by filtration over pyran - 2 - yloxy) - 9 - tribenzyl-siloxy - prosta - 5,13 - dien - 1 silica gel with diethylether/pentane (1:1). There were obtained 305 mg of the corresol, which was completely unitary accordponding urethane in the form of a colourless 15 ing to thin-layer chromatography. oil. The IR-spectrum (in chloroform) no longer 75 exhibited carbonyl vibration. IR (CHCl₃): 3470, 2943, 1700, 1650, 1020, 975 /cm. Example 38 (5Z,13E) - (8R,11R,12R,15S) - 1 - (N -Methylcarbamoyloxy) - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one. 300 mg of (5Z,13E) - (8R,11R,12R,15S) -250 mg of (5Z,13E) - (8R,9S,11R,12R,15S)-1 - (N - methyl - carbamoyloxy) - 11,15 - bis(tetrahydropyran - 2 - yloxy) - 9 - tribenzylsilyloxy - prosta - 5,13 - diene were stirred in 15 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) for 20 80 1 - (N - methylcarbamoyloxy) - 11,15 - bis-(tetrahydropyran - 2 - yloxy) - prosta - 5,13 dien - 9 - one were stirred with 9 ml of a 5 hours at 50°C, evaporated in vacuo and mixture of the glacial acetic acid/water/tetrahydrofuran (65/35/10) for 6 hours at 25 85 the residue was purified by chromatography over silica gel with diethylether/dioxane 40°C, and the mixture was then evaporated to (7+3). There were obtained 105 mg of the dryness in vacuo. After purifying the residue title compound in the form of a colourless oil. by chromatography over silica gel (diethylether/ethyl acetate 7+3) 145 mg of the title 90 30 IR (CHCl₃) compound were obtained in the form of a 3605, 3470, 2935, 1700, 1650, 1512, 1080, 972, 947 /cm. colourless oil. NMR (CDCl₃): IR (CHCl₃): δ 5.3—5.6 m, 4H olefinic protons. 3605, 3470, 2940, 1735, 1700, 1650, 3.8-4.3 m, 5H carbinolic proton and 35 1512, 1085, 972, 948 /cm. 95 $-CH_2-CH_2-O.$ The starting material for the above reaction was prepared as follows: 2.85 d, 6Hz (a) A solution of 370 mg of the 9,11,15 --NH— $-CH_3$. protected urethane prepared in accordance with Example 37 and 110 mg of 2.78 d, 7Hz 100 40 0.88 t 7Hz 3H, -CH2-CH3. tetrabutyl - ammonium fluoride in 30 ml of tetrahydrofuran was stirred for The starting material for the above reaction 2 hours at 0°C, the mixture was diluted was prepared as follows: with water, extracted with diethylether, (a) 1.80 Grams of prostaglandin F₂₀ methyl ester - 11,15 - bis - (tetrahydropyranyl) and the organic extract was agitated 105 with brine, dried over magnesium sul-45 ether (obtained from the corresponding phate and evaporated to dryness in vacuo. By filtration over silica gel with acid, see J. Amer. Chem. Soc. 91, 5675 (1969), with diazomethane) disdiethylether there were obtained 205 mg solved in 25 ml of pyridine were mixed with 1.40 grams of tribenylsilyl chloride, and the whole was stirred for 5 of (5Z,13E) - (8R,9S,11R,12R,15S) -110 1 - (N - methylcarbamoyloxy) - 11,15 -50 bis (tetrahydropyran - 2 - yloxy) hours at 50°C under argon. After prosta - 5,13 - dien - 9 - ol in the form distilling off the solvent in vacuo, the of a colourless oil. oily residue was chromatographed over silica gel with diethylether/pentane (b) To a solution of 290 mg of the 9 -115 hydroxy - compound obtained above in 55 mixtures. There were obtained 2.05 8 ml of acetone was added dropwise at 20°C 0.25 ml of Jones reagent, and grams of the corresponding 9 - tribenzylsilyl ether in the form of a colourthe whole was stirred for 25 minutes at

-20°C, the excess of reagent was de-

composed by the addition of isopro-

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panol, and the mixture was diluted with diethylether and agitated until neutral with brine. After drying over magnesium sulphate and evaporating, there were obtained 265 mg of (5Z,13E) -(8R,11R,12R,15S) - 1 - (N - methyl-carbamoyloxy) - 11,15 - bis(tetrahydropyran - 2 - yloxy) - prosta - 5,13 dien - 9 - one in the form of a colourless oil.

IR, CHCl₃): 3470, 2945, 1735, 1700, 1650, 1080, 972, 948 /cm.

Example 39

(5Z,13E) - (8R,12S,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

250 mg of the PGE-derivative prepared in accordance with Example 38 in 16 ml of acetic acid of 90% strength were stirred for 16 hours at 60°C, evaporated in vacuo, and the residue was purified by preparative layer chromatography (silica gel, diethylether). 165 mg of the title compound were obtained in the form of a colourless oil.

IR (CHCl₃): 3600, 3500 (wide), 2940, 1700, 1602, 978 /cm.

To a solution of 405 mg of the 1-alcohol

Example 40 (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(N - 1)]Methane - sulphonyl) - carbamoyloxyl prosta - 5,13 - dien - 9,11,15 - triol.

obtained in accordance with Example 37(b) in 10 ml of absolute toluene were added at 0°C 145 mg of methane - sulphonyl isocyanate, and the whole was stirred for 1 hour at 20—25°C, water was added, the mixture was extracted by agitation with diethylether, and the extract was washed with brine, dried over magnesium sulphate and evaporated in vacuo. After filtering the residue over silica gel with methylene chloride there were obtained 390

mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1 -[(N - methane - sulphonyl) - carbamoyloxy] - 11,15 - bis(tetrahydropyran - 2 - yloxy) - 9 tribenzyloxy - prosta - 5,13 - diene in the form of a colourless oil.

From 300 mg there were obtained in the manner analogous to that in Example 37 120 mg of the title compound in the form of a colouriess oil.

IR (CHCl₃): 3600, 3380, 1720, 1400, 1346, 1020, 975 /cm.

Example 41 (5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - 1)]Methane - sulphonyl) - carbamoyloxy] -11,15 - dihydroxy - prosta - 5,13 - dien 9 - one.

In a manner analogous to that in Example

38 there were obtained from 250 mg of (5Z,13E) - (8R,11R,12R,15S) - 1 - [(N methane - sulphonyl) - carbamoyloxy] 11,15 - bistetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 9 - one 112 mg of the 65 title compound in the form of a colourless oil.

IR (CHCl₃): 3600, 3400, 2940, 1735 (shoulder), 1720, 1400, 1345, 1020, 976 /cm.

The starting material for the above reaction was obtained as follows:

(a) In a manner analogous to that in Example 38(a) there were obtained from 400 mg of the 9 - tribenylsilyloxy-compound prepared in accordance with Example 40 and 120 mg of tetrabutyl-ammonium fluoride 210 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1 -[(N - methane - sulphonyl) - carbamoyloxy] - 11,15 - bis(tetrahydropyran - 2 - yloxy) - prosta - 5,13 dien - 9 - ol in the form of a colourless oil.

(b) In a manner analogous so that in Example 38(b) there were obtained from 210 mg of the compound prepared as above and 0.2 ml of Jones reagent 170 mg of (5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - methane - sulphonyl) - carbamoyloxy] - 11,15 - bis(tetrahydro-90 pyran - 2 - yloxy) - prosta - 5,13 dien - 9 - one in the form of a colourless oil.

Example 42 (5Z,13E) - (8R,12S,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy prosta - 5,10,13 - trien - 9 - one.

200 mg of PGE-derivative prepared in accordance with Example 41 in 12 ml of acetic acid of 90% strength were stirred for 16 hours at 60°C, the mixture was evaporated in vacuo, and the residue was purified by preparative layer chromatography (silica methylene chloride/isopropanol 9+1). gel, 105 mg of the title compound were obtained in the form of a colourless oil.

IR (CHCl₂): 3600, 3500, 2944, 1710, 1603, 978 /cm.

WHAT WE CLAIM IS: -1. A compound of the general formula I

in which

R₁ represents an acyl group of an organic carboxylic or sulphonic acid containing 1 to 15 carbon atoms or a group obtain-

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100

able from an oxygen-containing inorganic acid by the removal of a hydroxyl group, R₂ and R₃ each represents a hydrogen atom or an alkyl group containing 1 to 4 car-5 bon atoms. represents a $-CH_2-CH_2$, co--CH = CH— or trans -CH=CH-B represents a -CH₂-CH₂-, trans 10 —CH=CH— or —C≡C— group or a group, in which the methylene group is α - or β -positioned, W represents a free, esterified or etherified 15 hydroxy - methylene group, the hydroxyl group being in the α - or β -position, a free or ketalised carbonyl group or a group of the formula 20 in which R, represents a free, esterified or etherified hydroxyl group in the α - or β -position. D and E together represent a direct bond, 25 D represents a straight chained or branched alkylene group containing 1 to 5 carbon atoms or a —C≡C— group and E represents an oxygen or sulphur atom or a direct bond, 30 R4 represents an unsaturated aliphatic hydrocarbon group, an optionally C1-4alkyl-substituted cycloalkyl group, optionally substituted aryl-aliphatic hydrocarbon group, an optionally substituted 35 aryl group, a benzodioxol - 2 - yl group or a monocyclic heterocyclic group and, when D and E together represent a direct bond, or D represents a straight chained or branched alkylene group containing 1 to 5 carbon atoms or a —C≡C— group 40 and E represents an oxygen or sulphur atom or D represents a —C≡C— group and E represents a direct bond, may also represent an alkyl group, 45 Z represents a carbonyl or a free, esterified or etherified hydroxymethylene group, and X----Y,

when Z represents a free, esterified or etherified hydroxymethylene group, represents a

-GH - CH-

22 group, in which the methylene group is α - or β -positioned, or a group of the 55 -CH2-C- or -CH2-CHin which R_s represents an alkyl group or a free esterified or etherified hydroxyl group, or, 60 when Z represents a carbonyl group, represents a group of the formula -CH = CH -OF -CH₂---CH---, 65 R', in which R's represents an alkyl group or a free or etherified hydroxyl group. 2. A compound of the general formula I given in claim 1, in which R1 represents a 70 group of the formula -NH--R.. U represents an oxygen or sulphur atom and R₆ represents an optionally substituted alkyl, cycloalkyl, aryl or heteroaryl group or an acyl group of an organic 75 carboxylic or sulphonic acid, and R₃, R₂, A, B, W. D. E, R₄, Z and 80 have the meanings given in claim 1.

3. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 -Acetoxy - prosta - 5,13 - dien - 9,11,15 triol. 4. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 -85 Isobutyryloxy - prosta - 5,13 - dien - 9,11,15 -5. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 -Benzoyloxy - prosta - 5,13 - dien - 9,11,15 -90 6. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 -Butyryloxy - prosta - 5,13 - dien - 9,11,15 triol. (5Z,13E - (8R,9S,11R,12R,15S) -- (Decanoyloxy - prosta - 5,13 - dien -95 9,11,15 - triol. 8. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 -[(Methoxy) - acetoxy] - prosta - 5,13 - dien -9,11,15 - triol.

9. (5Z,13E) - (1RS,8R,9S,11R,12R,15S) -

10. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 1,1 - dimethyl - prosta - 5,13 -

11. (5Z,13E) - (8R,9S,11R,12R,15S) - 1

1 - Acetoxy - 1 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

dien - 9,11,15 - triol.

100

	Acetovy - 15 - methyl procts 5 12 diam	21 /57 12E) /0D 11D 12D 15C) 1	
	Acetoxy - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.	31. (5Z,13E) - (8R,11R,12R,15S) - 1 -	
	12. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 -	Acetoxy - 15 - hydroxy - 11 - methyl - prosta - 5,13 - dien - 9 - one.	
	Acetoxy - 16 - phenoxy - 17,18,19,20 - tetra-	32. (5Z,13E) - (8R,11R,12R,15R) - 1 -	
5	nor - prosta - 5,13 - dien - 9,11,15 - triol.	Acetoxy - 11,15 - dihydroxy - 16,16 - di-	70
_	13. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 -	methyl - prosta - 5,13 - dien - 9 - one.	
	Acetoxy - 16 - (3 - trifluoromethylphenoxy) -	33. (5Z,13E) - (8R,12S,15S) - 1 - Acetoxy -	
	17,18,19,20 - tetranor - prosta - 5,13 - dien -	15 - hydroxy - prosta - 5,10,13 - trien - 9 -	
	9,11,15 - triol.	one.	
10	14. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 -	34. (5Z,13E) - (8R,12S,15S) - 1 - Acetoxy -	75
	Acetoxy - 16 - (4 - chlorophenoxy) -	15 - hydroxy - 15 - methyl - prosta -	
	17,18,19,20 - tetranor - prosta - 5,13 - dien -	5,10,13 - trien - 9 - one.	
	9,11,15 - triol.	35. (5Z,13E) - (1RS,8R,9S,11R,12R,15S) -	
15	15. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 17 - phenyl - 18,19,20 - trinor -	1,9,11,15 - Tetracetoxy - 1 - methyl - prosta -	90
13	prosta - 5,13 - dien - 9,11,15 - triol.	5,13 - diene.	80
	16. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 -	36. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16,16 - di-	
	Acetoxy - 11 - methyl - prosta - 5,13 - dien -	methyl - prosta - 5,13 - dien - 9,11,15 - triol.	
	9,15 - diol.	37. (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 -	
20	17. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 -	Carboxy - propionyloxy) - 11,15 - dihydroxy -	85
	Acetoxy - 16,16 - dimethyl - prosta - 5,13 -	16,16 - dimethyl - prosta - 5,13 - dien - 9 -	
	dien - 9,11,15 - triol.	one.	
	18. (5Z,13E) - (8R,11R,12R,15S) - 1 -	38. (5Z,13E) - (8R,12R,15R) - 1 - (2 -	
26	Acetoxy - 11,15 - dihydroxy - prosta - 5,13 -	Carboxy - propionyloxy) - 15 - hydroxy -	
25	dien - 9 - one.	16,16 - dimethyl - prosta - 5,10,13 - trien -	90
	19. (5Z,13E) - (8R,11R,12R,15S) - 1 - Iso- butyryloxy - 11,15 - dihydroxy - prosta -	9 - one.	
	5,13 - dien - 9 - one.	39. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - prosta - 5,13 -	
	20. (5Z,13E) - (8R,11R,12R,15S) - 1 -	dien - 9,11,15 - triol.	
30	Benzoyloxy - 11,15 - dihydroxy - prosta -	40. (5Z,13E) - (8R,11R,12R,15S - 1 -	95
	2,13 - dien - 9 - one.	(N - Methylcarbamoyloxy) - 11,15 - di-	
	1. (5Z,13E) - (8R,11R,12R,15S) - 1 -	hydroxy - prosta - 5,13 - dien - 9 - one.	
	Decanoyloxy - 11,15 - dihydroxy - prosta -	41. $(5Z,\overline{1}3E) - (8R,12S,15S) - 1 - (N -$	
2.5	5,13 - dien - 9 - one.	Methylcarbamoyloxy) - 15 - hydroxy - prosta -	
35	22. (5Z,13E) - (8R,11R,12R,15S) - 1	5,10,13 - 9 - one.	100
	Butyryloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.	42. (5Z,13E) - (8R,9S,11R,12R,15S) - 1	
	23. (5Z,13E) - (8R,11R,12R,15S) - 1 -	[(N - Methane - sulphonyl) - carbamoyloxy] - prosta - 5,13 - dien - 9,11,15 - triol.	
	[(Methoxy) - acetoxy] - 11,15 - dihydroxy	43. (5Z,13E) - (8R,11R,12R,15S) - 1 -	
40	prosta - 5,13 - dien - 9 - one.	[(N - Methane - sulphonyl) - carbamoyloxy] -	105
	24. (5Z,13E) - (8R,11R,12R,15S) - 1 -	11,15 - dihydroxy - prosta - 5,13 - dien - 9 -	
	Acetoxy - 11,15 - dihydroxy - 1 - methyl -	one.	
	prosta - 5,13 - dien - 9 - one.	44. $(5Z,13E) - (8R,12S,15S) - 1 - [(N -$	
4.5	25. (5Z,13E) - (8R,11R,12R,15S) - 1 -	Methane - sulphonyl) - carbamoyloxy] - 15 -	
45	Acetoxy - 11,15 - dihydroxy - 1,1 - dimethyl -	hydroxy - prosta - 5,10,13 - trien - 9 - one.	110
	prosta - 5,13 - dien - 9 - one. 26. (5Z,13E) - (8R,11R,12R,15S) - 1 -	45. Any one of the compounds as claimed	
	Acetoxy - 11,15 - dihydroxy - 15 - methyl -	in claim 1 and described in Examples 1 to 10, 34, 35, 37, 38, 40 and 41 herein, exclud-	
	prosta - 5,13 - dien - 9 - one.	ing the compounds claimed in claims 3 to 12,	
50	27. (5Z,13E) - (8R,11R,12R,15R) - 1 -	36, 37, 39, 40, 42 and 43.	115
	Acetoxy - 11,15 - dihydroxy - 16 - phenoxy -	46. A process for the manufacture of a	
	17,18,19,20 - tetranor - prosta - 5,13 - dien -	compound as claimed in claim 1, wherein a	
	9 - one.	compound of the general formula II	
	28. (5Z,13E) - (8R,11R,12R,15R) - 1 -	.	
55	Acetoxy - 11,15 - dihydroxy - 16 - (3 - tri-	2	
	fluoromethylphenoxy) - 17,18,19,20 - tetranor -	R ₇ L _R	
	prosta - 5,13 - dien - 9 - one.) (II)	
	29. (5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - (4 -	I mannerat	
60	chlorophenoxy) - 17,18,19,20 - tetranor -	in which	120
	prosta - 5,13 - dien - 9 - one.	A, Z,	
	30. (5Z,13E) - (8R,11R,12R,15S) - 1 -	x <u></u> Y,	
	Acetoxy - 11,15 - dihydroxy - 17 - phenyl -		
	18,19,20 - trinor - prosta - 5,13 - dien -	B, W, D, E, R ₂ , R ₃ and R ₄ have the	
65	9 - one.	meanings given in claim 1, is esterified	

5	in the 1-position, if desired after protecting any other free hydroxyl group present, and then, if desired, in the resulting compound any protected hydroxyl group is liberated and/or any free hydroxyl group is oxidized or esterified and/or any free keto group is ketalised or reduced and/or any double bond is hydrogenated or methylated and/or by	52. A pharmaceutical preparation which comprises a compound as claimed in claim 1, in admixture or conjunction with a pharmaceutically suitable carrier. 53. A pharmaceutical preparation which comprises a compound as claimed in claim 2, in admixture or conjunction with a pharmaceutically suitable carrier. 54. A pharmaceutical preparation which	55
10	splitting off water in the 10,11-position from an 11 - hydroxy - 9 - oxo - compound a double bond is introduced, and/or, if desired, any epimers are separated.	comprises the compound claimed in any one of claims 3 to 35, in admixture or conjunction with a pharmaceutically suitable carrier. 55. A pharmaceutical preparation which	6:
15	47. A process for the manufacture of a compound as claimed in claim 2, wherein a compound of the general formula II given in claim 46, in which	of claims 36 to 38, in admixture or conjunction with a pharmaceutically suitable carrier. 56. A pharmaceutical preparation which comprises the compound claimed in any one of claims 30 to 44 in admiratory or conjunction.	70
20	A, Z, $x_{}$, B, W, D, E. R_2 , R_3 and R_4 have the	of claims 39 to 44, in admixture or conjunction with a pharmaceutically suitable carrier. 57. A preparation as claimed in any one of claims 52 to 56, which is in the form of a	70
25	meanings given in claim 1, is esterified in the 1-position, if desired after protecting any other free hydroxyl group present, and then, if desired, in the resulting com- pound any protected hydroxyl group is	sterile aqueous solution containing the active substance in an amount of 0.01 to 10 μ grams per ml. 58. A preparation as claimed in any one of claims 52 to 56, which is in form suitable	75
30	liberated and/or any free hydroxyl group is oxidized or esterified and/or any free-keto group is ketalised or reduced and/or any double bond is hydrogenated or methylated and/or by splitting off water	for inhalation. 59. A preparation as claimed in claim 58, which is in the form of an aerosol or spray solution. 60. A preparation as claimed in any one call.	80
35	in the 10,11-position from an 11 - hydroxy - 9 - oxo - compound a double bond is introduced, and/or, if desired, any epimers are separated.	claims 52 to 56, which is in a form suitable for oral administration. 61. A preparation is claimed in claim 60, which is in the form of a tablet, dragée or	85
40	48. A process as claimed in claim 46 or 47, conducted substantially as described herein. 49. A process for the manufacture of a compound as claimed in claim 1, conducted substantially as described in any one of Examples	capsule. 62. A preparation as claimed in any one of claims 52 to 56, which is in a form suitable for parenteral administration. 63. A preparation as claimed in claim 62, which is in the form of a sterile aqueous or	90
45	1 to 33 herein. 50. A process for the manufacture of a compound as claimed in claim 1, conducted substantially as described in any one of Examples 34 to 36 herein. 51. A process for the manufacture of a	oily solution suitable for injection. ABEL & IMRAY, Chartered Patent Agents, Northumberland House,	
50	compound as claimed in claim 2, conducted substantially as described in any one of Examples 37 to 42 herein.	303—306, High Holborn, London, WC1V 7LH.	

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